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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/714,792	11/16/2000	Mary Collins		3965

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EXAMINER	
HAMUD, FOZIA M	

ART UNIT	PAPER NUMBER
1647	

DATE MAILED: 06/08/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/714,792	COLLINS ET AL.	
	Examiner	Art Unit	
	Fozia M. Hamud	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 December 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *18,41,46-49,51,53-57,59,61-65,67,69,78-81,83,85-94 and 96-131* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *18,41,53,61-65,67,69,78-81,83,85-87 and 96-131* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) *46-49, 51, 54-57, 59, 88-89, 91-94* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *09/13/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Response to Amendment

1a. Receipt of Applicants' response, filed on 27 December 2004 is acknowledged.

1b. Applicant's request for the withdrawal of the advisory action mailed on 07 December 2004 is granted. Furtherrmore, upon further consideration, the examiner has decided to withdraw the finality of the previous office action (mailed on 20 April 2004). PROSECUTION IS HEREBY REOPENED.

1c. The indicated allowability of claims 97-100 is hereby withdrawn, in light of the following new rejections.

1d. Claims 1-17, 19-40, 42-45, 50, 52, 58, 60, 66, 68, 70-77, 82, 84, 95 have been cancelled, new claims 105-131 have been added. Thus claims 18, 41, 46-49, 51, 53-57, 59, 61-65, 67, 69, 78-81, 83, 85-94, 96-131 are pending and under consideration.

1e. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

2. The following previous objections and rejections are withdrawn in light of Applicants amendment filed 09/13/04.

(I) The obviousness-type double patenting rejection made against claim 41, 53,61, 69, 85, 87 and 96 as being unpatentable over claim 1 of U.S. Patent No. 6,248,714, is withdrawn. Applicants' argument that using an antibody that binds to SEQ ID NO:4 to inhibit the binding of IL-13 to IL-13 receptor and using the protein of SEQ ID NO:4 itself to inhibit said binding, are patentably distinct inventions, is found persuasive.

(II) All of the rejections against cancelled claims 50, 52, 60, 68, 84 and 95, are moot.

(III) The rejection of claims 89-96, made under 35 U.S.C. 112, first paragraph, is withdrawn, because an antibody that binds to a variant of the IL-13 bc comprising at least 95% identity to the amino acid sequence set forth in SEQ ID NO:4, wherein said variant binds to IL-13, can be made and used by one of ordinary skill in the art. One of ordinary skill in the art can generate antibodies that bind to a polypeptide that shares at least 95% identity to the polypeptide of SEQ ID NO:4, and it would not constitute undue experimentation to test whether said variant binds to IL-13.

Response to Applicants' arguments:

Claim Rejections under 35 U.S.C. §112:

3. Claims 62-65, 67, 69, 78-81, 83, 85, 101-102 stand rejected and new claims 115-119, 130-131 are rejected under 35 U.S.C. §112, first paragraph for not enabling the scope of the claimed invention, for reasons of record set forth in the office actions mailed on 08/18/03 and 04/20/04.

Applicants argue that the Examiner has not established that those skilled in the art would not know which direction to experiment, neither has the Examiner established that random experimentation is considered undue in this art. Applicants contend that it was routine in the art to generate, evaluate and test IL-13-binding fragments at the time the instant application was filed. Thus, Applicants conclude that since the instant specification discloses the extracellular domain of IL-13bc as amino acid residues 26-341 of SEQ ID NO:4, and since the specification provides how to test for biological activities, testing which fragments that retain the specified binding affinity is not undue experimentation.

These arguments have been considered, but are not deemed persuasive. Firstly, claim 62 is drawn to an antibody that binds to a fragment of IL-13bc, however, the instant specification discloses that the human IL-13bc as comprising the amino acid sequence set forth in SEQ ID NO:4, while the murine IL-13bc as comprising the amino acid sequence set forth in SEQ ID NO:2. Therefore, an antibody that binds to a fragment of human IL-13bc is distinct from an antibody that binds to a fragment of murine IL-13bc. Furthermore, the instant specification does not disclose an enabling disclosure of "all" the possible IL-13bc proteins. Thus, although an isolated antibody that binds to a fragment of the IL-13bc comprising the amino cid sequence set forth in SEQ ID NO:4, wherein said fragment binds to IL-13 at the recited kD, is enabled, an antibody that binds to "all possible" IL-13bc is not enabled.

Regarding claim 78 and the claims that depend from it, the instant specification does not disclose variants of IL-13bc encoded by a nucleic acid which hybridizes to SEQ ID NO:3. The specification discloses that SEQ ID NO:3 encodes the protein of SEQ ID NO:4, therefore, a nucleic acid that hybridizes to SEQ ID NO:3 (i.e the complement of SEQ ID NO:3) would not be expected to encode the polypeptide of SEQ ID NO:4.

Although it was routine to generate antibodies against desired proteins, at the time that the instant application was filed, generating antibodies against variants of proteins, which retained the desired activity encompassed undue experimentation. Since the amino acid sequence of a protein determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid

sequence and obtain the desired activity requires substantial guidance with respect to which amino acids in the protein's sequence, if any, would tolerate to modification, and detailed knowledge of the ways in which protein's structure relates to its function. In addition, making "conservative" substitutions does not usually produce predictable results. See, for example Lazar et al (Mol. Cell. Biol., Vol. 8, pp. 1247-1252, 1988(U)) who teach that the conservative substitution of glutamic acid for aspartic acid at position 47 reduced biological function of transforming growth factor alpha, while "nonconservative" substitutions with alanine or asparagine had no effect (see at least the Abstract). In the absence of such guidance, one skilled in the art would have to proceed with undue trial and error experimentation to screen through a vast number of fragments of the polypeptide of SEQ ID NO:4 to identify those fragments having the functional activity of SEQ ID NO: 4, and then generate antibodies against them.

Finally, it is noted that while patent need not teach, and preferably omits what is well known in the art, the Federal Circuit has cautioned against over-reliance on the rule, cited by Applicant. See Genentech Inc. v. Novo Nordisk A/S, 108 F.3d 1361, 1366, 42 USPQ2d 1001, 1005 (Fed. Cir. 1997): "[T]hat general, oft-repeated statement is merely a rule of supplementation, not a substitute for a basic enabling disclosure. It means that the omission of minor details does not cause a specification to fail to meet the enablement requirement. .... It is the specification, not the knowledge of one skilled in the art, that must supply the novel aspects of an invention in order to constitute adequate enablement". The Genentech court also held that [w]hile every aspect of a generic claim certainly need not have been carried out by an inventor, or exemplified in

the specification, reasonable detail must be provided in order to enable members of the public to understand and carry out the invention". Id. In this case, as in Genentech, the specification does not provide the "reasonable detail .....to enable members of the public to understand and carry out the invention".

New Rejections:

4. Claims 41, 53, 61, 69, 85, 87 and 96-131 are rejected under 35 U.S.C. §112, first paragraph, as failing to comply with the enablement requirement. The claims contain subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make practice the invention.

Claims 41, 53, 61, 69, 85, 87 and 96-131 are drawn to administration of a therapeutically effective amount of a composition comprising an antibody that specifically binds to IL-13bc, for the inhibition of the binding of IL-13 to the IL-13 receptor or for the treatment or inhibition of a specific condition. However, neither the instant specification nor the cited references of record, at the time the instant application was filed, taught a method of administering a therapeutically effective amount of a composition comprising an antibody that specifically binds to IL-13bc.

The instant specification discloses and the prior art at the time of filing recognized that IL-13 is a switch factor for IgE and IgG4, enhances B cell proliferation in the presence of CDL40 or anti-CD40 antibodies. Therefore, the role IL-13 plays in allergy and asthma was established. However, at the time the instant application was filed, there was no disclosure of the therapeutic administration of antibodies that bind to IL-

13bc. Although antibodies are excellent reagents to localize receptors, they are of little use as pharmacological agents. Antibodies have to be raised against the appropriate epitopes, in order to effectively interfere the ligand/receptor interaction. Moreover, anti-receptor antibodies can act both as agonists and as antagonists, depending on what conformational changes the antibody induces on the receptor, (see Mijares et al, Molecular Pharmacology, 2000, Vol.58, pages 373-379, especially abstract and page 377). In the instant case, Applicants do not disclose a method therapeutically administering an antibody that inhibits the binding of IL-13 to the IL-13 receptor. Therefore, the fact that IL-13 plays a role in allergy does not enable the claimed method of administering antibodies for therapeutic effect. The instant specification does not define "therapeutically effective amount", how much of the composition comprising an antibody that binds to IL-13bc is sufficient to treat cancer, allergy or asthma. Furthermore, there is no regimen of treatment disclosed. A patent is granted for a completed invention, not the general suggestion of an idea and how that idea might be developed into the claimed invention. In the decision of *Genentec, Inc, v. Novo Nordisk*, 42 USPQ 2d 100,(CAFC 1997), the court held that:

> "[p]atent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable" and that "[t]ossing out the mere germ of an idea does not constitute enabling disclosure". The court further stated that "when there is no disclosure of any specific starting material or of any of the conditions under which a process is to be carried out, undue experimentation is required; there is a failure to meet the enablement requirements that cannot be rectified by asserting that all the disclosure related to the process is within the skill of the art", "[i]t is the

specification, not the knowledge of one skilled in the art, that must supply the novel aspects of an invention in order to constitute adequate enablement".

The instant specification is not enabling because one can not following the guidance presented therein and practice the claimed method without first making a substantial inventive contribution.

Regarding new claims 105-131 the instant specification does not disclose a method of treating cancer by administering antibodies that bind to human IL-13bc of SEQ ID NO:4. Applicants submit post filing date references that demonstrate that IL-13Rbc is expressed in high levels in cancers such as glio or neurotblastomas and that anti-IL-13 Rbc antibodies might be useful. The instant specification contemplates that neutralizing or non-neutralizing antibodies binding to IL-1 3bc protein that are capable of blocking IL-I 3 binding to the IL- I 3bc may also be useful therapeutics for certain tumors and also in the treatment of other conditions. However, besides, these hypothetical suggestions, the specification fails to disclose that the actual administration of antibodies against IL-13bc resulted in the treatment of any condition. Therefore, the instant specification is enabling for a composition comprising an antibody that specifically binds to the IL-13 bc, said IL-13bc comprising the amino acid sequence set forth in SEQ ID NO:4, because one of ordinary skill in the art can make such an antibody and use it to purify the IL-13 bc or to study IL-13 bc properties. However, the instant specification is not enabling for a method of therapeutically administering an antibody that binds to IL-13bc, to inhibit the binding of IL-13 bc to IL-13 in vivo, or for the treatment or inhibition of allergic condition, or asthma, or to treat cancer in a mammal,

because it fails to disclose a single case where the administration of said antibody resulted in the treatment of any condition.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 78-81, 83, 85, 90, 101-102, 120-124 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

5a. Claim 78 is rejected as vague and indefinite, because the recited hybridization conditions are in complete, since only the wash conditions are recited. Furthermore, claim 78 recites the limitation "the" in line 1, before "antibody". There is insufficient antecedent basis for this limitation in the claim.

5b. Claim 90 recites "the body", which renders the claim indefinite, because it is unclear which body is being referred to. It is suggested that "the antibody" be recited in the claim to obviate this rejection.

Claims 79-81, 83, 85, 86, 101-102 and 120-124 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite, so far as they depend on claims 18 and 78 for the limitations set forth directly above.

Conclusion:

6. Claims 46, 47, 48, 49, 51, 54, 55, 56, 57, 59, 86, 88, 89 and 91-94 are allowable.

Advisory Information:

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Fozia M. Hamud whose telephone number is (571) 272-

0884. The examiner can normally be reached on Monday, Thursday-Friday, 6:00 am to 4:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda G. Brumback can be reached on (571) 272-0961. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Fozia Hamud
Patent Examiner
Art Unit 1647
03 June 2005

JANET ANDRES
PRIMARY EXAMINER